

**REMARKS**

**A. The Status of the Claims and the Amendments**

By the present amendment, claim 1 has been canceled without prejudice and was essentially replaced by the new claim 105. Claims 2-104 were previously canceled. The Applicants acknowledge the fact that the restriction requirement having been made final.

New claims 105-116 have been added. No new matter have been introduced in the amendments to the pending claims or with the new claims. Accordingly, entry of the amendment is respectfully requested. Upon entry of this amendment, claims 105-116 will be under consideration.

**B. Rejections Under 35 U.S.C. § 102(b)**

Claim 1 stands rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by the following nineteen references (see, items 6-21, pages 3-11 of the Office Action):

- (1) U.S. Patent No. 3,039,929 to Stanko ("Stanko");
- (2) U.S. Patent No. 3,689,638 to Harth et al. ("Harth");
- (3) U.S. Patent No. 3,885,028 to Cella et al. ("Cella");
- (4) U.S. Patent No. 3,957,964 to Grimm ("Grimm");
- (5) U.S. Patent No. 4,152,418 to Pader ("Pader '418");
- (6) U.S. Patent No. 4,178,362 to Pader ("Pader '362");
- (7) U.S. Patent No. 3,050,443 to Kraus ("Kraus");
- (8) U.S. Patent No. 3,073,743 to Spero ("Spero");

- (9) U.S. Patent No. 3,891,757 to Higuchi ("Higuchi");
- (10) U.S. Patent No. 3,823,229 to Jederstrom ("Jederstrom");
- (11) U.S. Patent No. 4,044,126 to Cook et al. ("Cook '126");
- (12) U.S. Patent No. 4,364,923 to Cook et al. ("Cook '923");
- (13) U.S. Patent No. 4,414,209 to Cook et al. ("Cook '209");
- (14) U.S. Patent No. 4,211,771 to Witkowski et al. ("Witkowski");
- (15) U.S. Patent No. 4,689,213 to Golub et al. ("Golub");
- (16) U.S. Patent No. 5,240,694 to Gwaltney ("Gwaltney");
- (17) U.S. Patent No. 5,292,513 to Gristina et al. ("Gristina");
- (18) U.S. Patent No. 5,558,664 to Sarzaud et al. ("Sarzaud"); and
- (19) U.S. Patent No. 6,436,368 to Love et al. ("Love").

These rejections are respectfully traversed.

Claim 1 has been canceled without prejudice and essentially replaced by the new claim 105. The following discussion is, therefore, directed mainly to the new claim 105.

It is axiomatic that a valid rejection of a claim for anticipation by a reference requires that the reference explicitly or inherently describe all of the elements, limitations, and relationships recited in the claim. In addition, a valid 102(b) reference must have the publication date that is more than 1 year prior to the earliest priority date of claims in question. It is submitted that none of the above-described references teaches all the elements and limitations recited in the new claim 105.

In particular, claim 105 recites a method of delivery of a composition which comprises "the protein compound to be delivered and an organic halide," wherein the halide is a member of a Markush group recited in claim 105. None of the references cited by the Examiner either directly describe or suggest delivering a composition having the above-mentioned features.

More specifically, with respect to the first cited reference, Stanko discloses the use of fluorinated hydrocarbons for the delivery of isoproterenol. There is nothing in Stanko teaching or suggesting the delivery of any protein, as required by claim 105. Isoproterenol is an alcohol, not a protein, as clearly taught by Stanko (col. 1, lines 15-18).

With respect to the second, third, fourth, fifth, and sixth cited references, each of Harth, Cella, Grimm, Pader '418 and Pader '362 teaches the use of chloroform and enzymes, but none of these references teaches or suggests using any organic halide recited in claim 105. Chloroform (i.e., trichloromethane) is not one of the halides recited in claim 105.

With respect to the seventh cited reference, Kraus discloses the use of Freon 12 in combination with ammonia and chloroform for headache relief. There is nothing in Kraus describing or suggesting the use of any proteins, as required by claim 105.

With respect to the eighth cited reference, Spero discloses the use of both freons and chlorinated butanol for delivering active components to various tissues, such as respiratory tissues. For example, Spero teaches that acetamide can be such an active component. There is nothing in Spero describing or suggesting the use of any proteins as active components, as required by claim 105.

With respect to the ninth cited reference, Higuchi discloses the use of certain halogenated solvents for the delivery proteins such as insulin. Higuchi fails to teach or suggests using any organic halide recited in claim 105. Halogenated hydrocarbons that

Higuchi does describe (i.e., trichloro- and trifluoroethanol) are not among the halides recited in claim 105.

With respect to the tenth cited reference, Jederstrom discloses the use of fluorinated hydrocarbons for the delivery of 7-( $\beta$ -hydroxypropyl)theophylline in an aqueous alcohol carrier. There is nothing in Jederstrom teaching or suggesting the delivery of any protein, as required by claim 105. Theophylline is, of course, not a protein, but rather an aromatic heterocyclic compound, i.e., 1,3-dimethyl-1H-purine-2,6(3H,7H)-dione.

With respect to the eleventh, twelfth, and thirteenth cited references, each of Cook '126, Cook '923, and Cook '209 teaches the use of methylene chloride, chlorofluorocarbons or chloroform for making asthma medications for delivery by inhalation. However, the only type of active compounds to be delivered that is taught or suggested in any of the three Cook references is steroids. There is nothing in any of Cook '126, Cook '923, and Cook '209 teaching or suggesting the delivery of any protein, as required by claim 105.

With respect to the fourteenth and fifteenth cited references, both Witkowski and Golub disclose the use of fluorinated hydrocarbons for the nasal delivery of various medications. Witkowski teaches the delivery of antiviral agents having the active ingredient 1-B-D-ribofuranosyl-1,2,4-triazole-3-carboxamide. Golub describes the delivery of calcium-channel blocking agents, such as gallopamil, which is chemically 5-[[2-(3,4-dimethoxyphenyl)ethyl]methylamino]-2-isopropyl-2-[3,4,5-trimethoxyphenyl]pentanonitrile hydrochloride. Neither the antiviral compounds of Witkowski nor the calcium-channel blocking agents of Golub are proteins. Accordingly, both Witkowski and Golub fail to teach or suggest the delivery of a protein, as required by claim 105.

With respect to the sixteenth cited reference, Gwaltney discloses the use of fluorinated hydrocarbons for the nasal delivery of various medications, such as antiviral

agents and anti-inflammatory compounds. Antiviral agents disclosed by Gwaltney include integerons, interferon inducers, capsid binding agents, benzoimidazoles, 1'-methyl spiro(adamantane-2,3-pyrrolidine)maleate, isatin thiosemicarbazone, fusidic acid, substituted trizaindoles, 2,6-diphenyl-3-methyl-2,3-dihydroimidazo[2,1-b]thiazole, 3-alpha-naphthyl-5-diethylcarbamoyl-1,2,4-oxadiazole, oxolinic acid, isoquinolines, 1-p-chlorophenyl-3-(m-3-isobutylguanidinophenyl)urea hydrochloride, anti ICAM-1 antibody synthetic ICAM-1, amantadine, rimantadine, and ribavirin. Anti-inflammatory compounds disclosed by Gwaltney include ipratropium, atropine methonitrate, exogenous opioid agonists, alpha adrenergic agonists, chlorpheniramine, prostaglandin blockers and antagonists, leukotriene blockers and antagonists, parasympathetic blockers and antagonists, and interleukin blockers and antagonists. None of the compounds to be delivered, as taught or suggested by Gwaltney include a protein, as required by claim 105.

With respect to the seventeenth cited reference, Gristina discloses the use of fluorinated hydrocarbons for delivery of various biocompatible particles to prime macrophages. Examples of the particles include opsonized zymosan, PMMA latex, and polystyrene. There is nothing in Gristina describing or suggesting the use of any proteins in the biocompatible particles to be delivered.

With respect to the eighteenth cited reference, Sarzau discloses the use of fluorinated hydrocarbons for delivery of various medications by transcutaneous drug administration, e.g., via a dermal patch. Examples of drugs to be delivered, as described by Sarzau include trinitrine, oestradiols and nicotine. Sarzau fails to describe or suggest that any proteins can be delivered via the dermal patch.

Finally, with respect to the nineteenth cited reference, Love teaches the use of fluorinated hydrocarbons for the delivery of asthma medications by inhalation. However, the only type of active compounds to be delivered that is taught or suggested by Love is

steroids (e.g., beclomethasone dipropionate). There is nothing in Love teaching or suggesting the delivery of any protein, as required by claim 105.

To summarize, some of the references cited by the Examiner describe the use of specific organic halides recited in claim 105, but fail to teach or suggest the use of any proteins. Some other references describe the delivery or active compounds based on proteins but fail to teach or suggest the use of any specific organic halides recited in claim 105. Some other references fail to teach or suggest both the use of specific organic halides and of proteins, as required by claim 105. None of the references describes or suggests both the use of specific organic halides and of proteins, as required by claim 105.

In view of the foregoing it is submitted that claim 105 is patentably distinguishable over all the cited references. Each of claims 106-116 depends on claim 105 and is therefore considered patentable for at least the same reason. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) are respectfully requested.

**C. Double Patenting Rejection**

Claim 1 stands rejected under the non-statutory, judicially created doctrine of obviousness-type double patenting over claims 1-4 of U.S. Patent No. 6,638,767 (item 22 on page 12 of the Office Action). Claim 1 has been canceled, and claim 105 has been added to replace claim 1.

While the Applicants respectfully traverse this rejection, it is believed that this issue has become moot in view of the cancellation of claim 1. Claim 105 that replaced claim 1 has a different scope, and is not believed to be within the purview of the double patenting rejection. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

**D. Objections**

The Examiner has objected to claim 1 on the ground that it included non-elected subject matter (see, item 4, on page 3 of the Office Action). More specifically, the Examiner has stated that amines, ketones and ethers are not the members of the elected group of halogenated alkyl chains.

The Applicants respectfully disagree. The election made by the Applicants on 08/18/06 in response to the restriction requirement (see the election requirement No. 2, page 13, lines 5-7 of the Office Action mailed 06/19/06) was for a "composition comprising a halogenated alkyl chain." It appears that the Examiner has interpreted the election to mean that only halogenated alkyls are elected. The election should not be read so restrictively. In fact, the Applicants' position is that any compound that includes a moiety that has halogenated alkyl chain is within the purview of the election.

With this in mind, the Applicants respectfully submit that no non-elected species are recited in the new claim 105 that has replaced the original claim 1. Indeed, all the amines (e.g., perfluorotributylamine or perfluorotripropylamine), ketones (e.g., 1,3-dichlorotetrafluoroacetone or 3-(trifluoromethoxy)-acetophenone) and ethers (e.g., perfluorobutylethyl ether or bis(perfluoroisopropyl) ether) that are recited in claim 105 do have halogenated alkyl chain(s). Finally, the Applicants respectfully remind that an inventor is always his own lexicographer. The Applicants accordingly defined amines, ketones and ethers having halogenated alkyl chain(s) as belonging to the category of organic halides (see, page 6, lines 16-21 and page 7, lines 24-28 of the original application). The Examiner should defer to the Applicants' definition.

In view of the foregoing, it is submitted that the objection does not apply. Accordingly, reconsideration and withdrawal of the objection are respectfully requested.

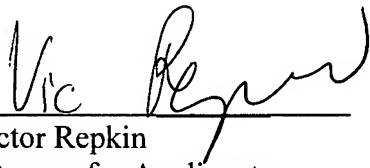
**CONCLUSION**

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Check number 586422 in the amount of \$510.00 is enclosed as payment for the Petition for Three-Month Extension of Time fee. No other fee is believed to be due in connection with filing this submission. However, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

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